Remarks

Claims 1 and 19-22, 24, 27-34, 36, and 39-48 are pending in the application. Claims 1, 19-21, 30-33 and 42-48 have been withdrawn from consideration pursuant to a restriction requirement. Claims 22, 24, 27-29, 34, 36 and 39-41 are under consideration and are rejected. Reconsideration is requested in view of the above changes and the following remarks.

Claims 22 and 34 have been amended. Support for the amendment is at paragraph 0019. The Office Action Summary of the May 17, 2010 office action indicates that the pending rejection is final. This is believed to be an error as the body of the office action does not indicate finality. This is consistent with PAIR, which indicates the mailing of a "Non-Final Rejection". Acknowledgement that the May 17 action is indeed non-final is respectfully requested.

Acknowledgement of Examiner Interview

Applicants thank Examiner Angela Scott for the courtesy extended during the telephonic interview of July 28, 2010 with the undersigned attorney. Claims 22 and 34 were discussed. The amendments to those claims, as presented above, were discussed. The prior art of record was discussed – Shalaby (US 2004/0133237). The arguments presented by applicants' attorney during the interview are as substantially recited below. The sketch appearing as part of this paper was also presented and discussed by applicants' attorney during the interview. No agreement as to allowability was reached.

Response to 35 USC §102 Rejection of Claims 22, 24 and 27-29

Claims 22, 24 and 27-29 have been rejected as being allegedly anticipated by Shalaby. The rejection alleges that Shalaby teaches an absorbable medical device, such as a suture, that is irradiated with an electron beam.

Shalaby (US2004/0133237) discloses biodegradable sutures and a tissue adhesive which have been exposed to gamma radiation to sterilize them, and also to reduce their molecular weight. Examples 1 to 3 are explicitly stated to be gamma irradiated (see [0013]), as is example 6 (see [0020]). Examples 4 and 5, and A and B, are on their face silent as to the type of radiation used. It is implicit that the process used is the same as that for Examples 1 to 3. Therefore, it is

clear that Examples 4 and 5, and A and B are also performed using gamma radiation for sterilization. There is no disclosure in Shalaby whatsoever of a specific article being irradiated with an electron beam, and the mention of an electron beam as an alternative to gamma radiation is clearly designed for use on articles that are so thin so as to be sterilizable without resort to the extremely high penetrating power of gamma radiation.

Shalaby is not concerned with forming articles having a gradient of bioabsorbability, but rather is concerned with providing fully sterilized articles which have a uniform bioabsorbability profile and breaking strain. It would in fact be undesirable for a gradient to be formed in the articles of Shalaby, as that would make it difficult to produce articles, *e.g.* sutures, of different thicknesses which have consistent properties. In Shalaby it is an advantage to have homogenous polymer properties throughout the article.

The Examiner is incorrect in his assertion that the articles of Examples 1 to 6 of Shalaby would inherently have a gradient of mass distribution and bioabsorbability from the entire outer surface to the core for a number of reasons, discussed as follows.

The penetration of gamma radiation is extremely high, typically having a half value layer of 1cm of lead or more. Gamma ray interactions with matter are entirely different from that of charged particles, i.e. electrons in the electron beam used in the present invention. The lack of charge in gamma rays eliminates coulomb interactions and allows gamma rays to be much more penetrating, i.e. very poorly absorbed. The interactions that do occur are by way of the photoelectric effect, Compton scattering, and pair production. This means that gamma rays are not rapidly absorbed by the first few millimetres or tens of millimetres of a substrate, with no rapid fall off as the beams penetrate further, as is the case with electron beam radiation. Thus gamma rays are not capable of providing a gradient in the manner of an electron beam, and certainly would produce no gradient in an article such as an implantable substrate.

The sutures of Shalaby have a total thickness of 0.5 mm or less (see tables II, III, IV, V and VII). The thickness of the sutures relative to the penetration of the gamma rays is so small that there would be effectively no change in intensity of the radiation across the thickness of the sutures, and therefore no gradient would be produced. If, for the sake of argument, any gradient

were produced it would be so negligible as to have absolutely no practical effect on bioabsorbability rates, and therefore would not be a gradient in a meaningful sense as required by the present invention.

The formation of a gradient in the present invention is dependent on irradiation of an article with electron beam radiation which has a relatively low penetration, typically in the order of a few millimeters to a few tens of millimeters. This is used to irradiate an article having dimensions commensurate with the penetration of the radiation such that a gradient through the thickness of the article is produced. This would not be achieved through the use of gamma rays as their absorption is so low that no suitable gradient would be produced.

For articles thicker than a suture, in line with the teaching of Shalaby, one skilled in the art would apply gamma radiation to the article. Given that Shalaby is principally concerned with sterilization of articles, then gamma rays would be actually be preferred for a thicker article, precisely because they have the higher penetration required to penetrate the entire article and fully sterilize it. Although Shalaby does speak to alteration to mass distribution and bioabsorbability, this is in the context of altering the entire thickness of the article; no discussion of a gradient is discussed or suggested. Even if the article irradiated in the method of Shalaby were tens of millimeters thick, the absorption of gamma rays is so low, as discussed above, that no gradient would be formed.

If the articles of Shalaby were exposed to electron beam radiation (even though this is not in fact disclosed in Shalaby) they are so thin that no meaningful gradient would be produced. Moreover, given that the object of Shalaby is to sterilize an article, not create a molecular weight distribution, the skilled artisan would understand from the disclosure of Shalaby that gamma radiation (which would produce no molecular weight gradient), not electron beam radiation, would be applied.

The skilled artisan would prefer to use gamma rays, as they are eminently suitable for sterilizing thicker articles, whereas there are significant technical barriers to using electron beam radiation. Electron beams have good penetrating power only at high energies (e.g. >10 MeV). Absent a good reason to shift from gamma rays to electron beam, the person skilled in the art

would use gamma rays. Thus, it would be counter-intuitive for the skilled person to move away from the gamma radiation used in the examples of Shalaby when a thicker article is being sterilized. The substrate of the present invention is irradiated with an electron beam because the desired effect is a molecular weight gradient, which can not be generated using gamma rays.

Accordingly, the practice of Shalaby, as implemented by one skilled in the art, would not result in the presently claimed substrate having a molecular weight distribution that changes gradually from the outer surface to the core in the nature of a gradient, as thick articles capable of generating such a gradient upon electron beam irradiation would never in fact be irradiated with electron beams. The skilled artisan would chose gamma radiation (which is incapable of forming a molecule weight gradient), since the skilled artisan would know that electron beam radiation would not provide sterilization of a thick article.

To further particularly point out and define the invention, the independent claims have been amended to recite that the average molecule weight at the core of the substrate is greater than the average molecular weight at the substrate *entire* outer surface.

Even if a gradient would be created using the teachings of Shalaby, which we contend would not happen, then it is apparent that such a gradient would not run from the entire outer surface to the core, as is required by the present claims. It is inherent from Shalaby that any gradient would run from the outer surface of the article proximate to the source of radiation, to the outer surface distal to the source of radiation. There is no disclosure in Shalaby of moving the surface of the suture relative to the radiation source. It is clear, therefore, that the radiation would be applied to the suture from a fixed angle. This could not result in an article in which the entire surface of the article has been irradiated to a higher level (and thus having its mass distribution reduced/bioabsorbability increased), as the core would actually receive a higher radiation dose than the distal surface. Such a gradient would not be within the ambit of the present clams. Furthermore, such a gradient would not be desirable as it would not allow for the controlled bioabsorption of the article from the outer surface toward the core. Figs 1 and 2 serve to illustrate the concepts discussed above, the gradient being illustrated by the shading used.

Fig 1: Shalaby

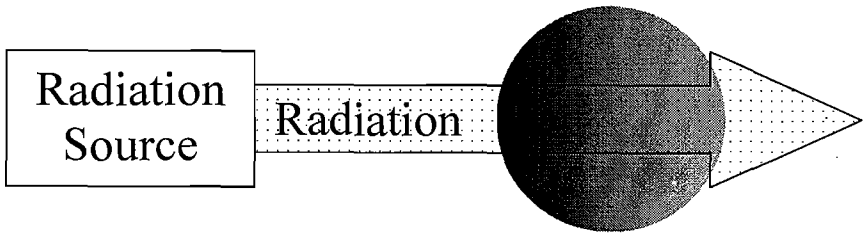
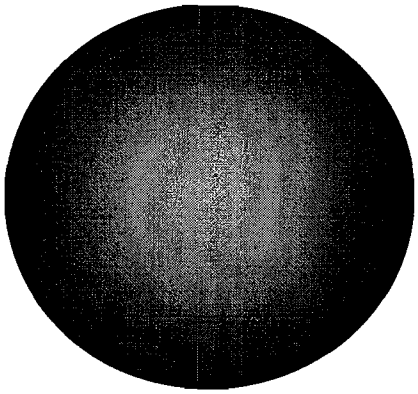


Fig 2: Present invention



The tissue adhesive disclosed in Shalaby cannot be considered to be a substrate or have a core or surface in the terms of the present claim; nor can it hold a gradient. The fluid adhesive is free to move around within its container and thus cannot have a permanent core or a surface. Any gradient that might be established in the adhesive would rapidly dissipate due to Brownian motion and/or diffusion. Thus this embodiment of Shalaby is in no way relevant to the teaching of the present invention.

Accordingly, it has been shown that the articles (sutures and adhesive) of Shalaby do not inherently comprise a gradient, as required in present claims. Furthermore, should the skilled artisan apply the teachings of Shalaby to other (thicker) articles, the artisan would be positively motivated to use gamma rays, not electron beam radiation. The former are inherently incapable of forming a gradient as required by the present invention.

Accordingly, the bioabsorbable, implantable substrate of claim 22 is novel and

nonobvious over Shalaby.

Claims 24 and 27-29 depend from claim 22, and recite additional features of the claimed substrate. In view of the allowability of claim 22, claims 24 and 27-29 are likewise allowable.

Response to 35 USC §102 Rejection of Claims 34, 36 and 39-41

Claims 34, 36 and 39-41 have been rejected as being allegedly anticipated by Shalaby. In the substrate of claim 22, at least a portion has been exposed to electron beam radiation to reduce the molecular weight distribution of that portion. In the substrate of claim 34, the entire surface is exposed to electron beam irradiation, to reduce the molecular weight distribution of the entire surface.

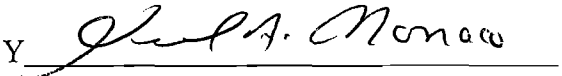
The substrate of claim 34 is novel and nonobvious over Shalaby for the same reasons as advanced above for claim 22. Claim 34, and its dependent claims 36 and 39-41 are allowable for Shalaby.

Conclusion

The claims remaining in the application are believed to be in condition for allowance. An early action toward that end is earnestly solicited.

Respectfully submitted,

FRASER JAMES BUCHANAN

BY 

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